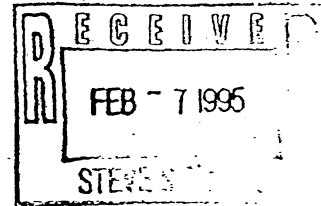


# **EXHIBIT A**

**Glaxo**

Timothy D. Proctor  
Senior Vice President, General Counsel & Secretary



February 6, 1995

J. Charles Wakerly, Esq.  
Senior Vice President, Director and  
General Counsel-U.S.  
SmithKline Beecham  
One Franklin Plaza  
P.O. Box 7929  
Philadelphia, PA 19101

*file  
zygon report*

Dear Mr. Wakerly:

The purpose of this letter is to advise you of Glaxo Inc.'s intent to pursue with FDA's Division of Drug Marketing, Advertising and Communications (DDMAC) and other appropriate government agencies several issues pertaining to the advertising and marketing of Kytril™ (granisetron HCL) Injection. I am advising you of this plan of action to provide SmithKline Beecham with the opportunity to address our concerns and thus preclude the need for FDA or other governmental involvement.

Our concerns relate to the following: 1) Inclusion of unapproved doses in Kytril promotional pieces. These pieces are also substantially lacking in fair balance. 2) Dissemination of false and misleading information, including comparative data pertaining to Zofran® (ondansetron HCL) through SKB sponsored symposium and speaker programs. 3) Distribution of "homemade" materials containing unsubstantiated cost comparisons and cost effectiveness claims. 4) Promotion of unapproved Kytril Tablets.

1. Promotion of Unapproved Kytril Doses

With few exceptions, Kytril promotional pieces such as Slim Jims, journal ads, and detail aids contain extensive references to an unapproved 40 mcg/kg dose of Kytril. As an example, a recently issued Slim Jim (copy attached as Exhibit A) presents data on page 2 which purports to reconfirm the "24-hour effectiveness [of Kytril] with a single 10 mcg/kg dose." Under this heading are two bar charts which present data on both the approved 10 mcg/kg dose as well as the 40 mcg/kg dose. Additional mentions of the 40 mcg/kg dose are included on pages 5, 6, and 7 of this piece. A similar pattern

J. Charles Wakerly, Esq.  
February 6, 1995  
Page 2

can be seen in an earlier Slim Jim (see Exhibit B) where data on the 40 mcg/kg dose is presented on pages 7, 9, 10, 11, and 12 as well as in journal ads for Kytril (see Exhibit C) where much of the same data is presented. It is our understanding from DDMAC that references to off-label doses are not permissible in promotional pieces.

We have also been advised by DDMAC that presentations providing efficacy parameters measured by antiemetic response rates must be fair balanced by inclusion of all data relating to failures. Failure rates have not been included with the presentations of the response rates for Kytril in either of the above-mentioned Slim Jims. This information has also been omitted from the Kytril journal ads. It therefore appears to us that substantially all Kytril promotional pieces are lacking in fair balance.

2. Distribution of Misleading "Homemade" Cost Comparisons

Glaxo's sales representatives have encountered a substantial amount of what appear to be "homemade" Kytril vs. Zofran cost comparisons. It is our understanding that many of these pieces have been generated through a company-provided lap top computer program. We are confident that DDMAC would agree with us that these pieces and the computer program through which some of them have been generated are objectionable for a number of reasons, including lack of accuracy, lack of references of sources of price data, the implication that Kytril and Zofran provide equal efficacy when no such support for such a claim is provided, and the lack of adequate disclaimers. (See July 19, 1994 Warning Letter from FDA to Eli Lilly and Company specifying required disclaimers for such price comparisons.) In addition, some of these homemade presentations, contrary to Kytril's labeling, promote the use of the single dose vial of Kytril as a multidose vial.

Other examples of these homemade cost comparison pieces include unsubstantiated product claims (see Exhibit D), stability data which is contrary to that provided in the PI (see Exhibit E), and unsubstantiated cost effectiveness claims (see Exhibit L). Another theme seen in these pieces is the promotion of unapproved doses for both Kytril and Zofran and statements that the products are equal in efficacy. Letters authored by your Drug Information Department are sometimes included with these materials which invariably lack both fair balance and complete prescribing information. These homemade pieces impose liability on SKB for the mislabeling of both Kytril and Zofran. In addition, a significant number of these pieces (see Exhibits F-J) contain direct statements or make references as to how institutions can increase their "profits" from Medicare through the use of Kytril. Some even go so far as to recommend that the medical professional use one vial of Kytril for two patients (see Exhibit F) but charge Medicaid for three vials. This raises significant fraud and abuse issues which I am sure you will want to investigate.

GWZ 313311

J. Charles Wakerly, Esq.  
February 6, 1995  
Page 3

A number of these improper price comparisons have been brought to our attention. Examples of nine of these comparisons are attached for your reference as Exhibits E-M with an additional three-four included in Exhibit N.

3. Dissemination of Misleading Data Through Symposium and Conferences Sponsored by SKB

We are also been made aware that SKB is disseminating much of the same information outlined in number 1 above through company-sponsored symposium and conferences. As an example, attached as Exhibit O are copies of the invitation and slides from a conference entitled "Efficacy and Safety of Granisetron in the Prophylaxis of Acute Nausea and Vomiting Induced by Chemotherapy". The invitation is on SKB letterhead and indicates that the guest speaker will be Dr. Carl J. Friedman, Group Director, Clinical Investigation, SmithKline Beecham Pharmaceuticals. Dr. Friedman's slides include data on the 40 mcg/kg dose and other unapproved doses of 5, 20, and 160 mcg/kg and data on complete response rates which does not include information on failures. These slides also include comparisons between the combination of metoclopramide and dexamethasone versus the combination of chlorpromazine and dexamethasone as antiemetic agents. Labeling for these products do not include approval for combination therapy in the treatment of cancer chemotherapy induced emesis. The slide presentation also includes unreferenced price information on Zofran. Presentation of false and misleading information through company-sponsored "scientific exchanges" was the subject of a recent Warning Letter to Burroughs Wellcome [see December 1, 1994 letter to Burroughs Wellcome concerning Lamictal (lamotrigine) Tablets].

A more extensive body of misleading information is presented in an SKB-sponsored program entitled "Chemotherapy Induced Nausea and Vomiting-Past and Present" (see Exhibit P). This presentation is objectionable because it raises many of the same issues described above: unsupported superiority claims, references to unapproved combination therapy, and unapproved doses for both Zofran and Kytril, and a lack of fair balance. Since this symposium does not appear to satisfy FDA's Draft Policy on Industry Supported Scientific and Educational Activities, all of these slides are promotional labeling and violate FDA's rules on promotion.

4. Promotion of Unapproved Tablet Form of Kytril

We have most recently been made aware of the fact that SKB representatives are promoting Kytril Tablets. An article entitled "Oral granisetron alone and in combination with dexamethasone: A double-blind randomized comparison against high-dose metoclopramide plus dexamethasone in prevention of cisplatin-induced emesis," attached as Exhibit Q, was delivered to a health care professional by an SKB

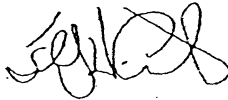
GWZ 313312

J. Charles Wakerly, Esq.  
February 6, 1995  
Page 4

representative last month. Also in November, during a presentation sponsored by SKB at an "Oncology Nurses Appreciation Night" in Omaha, Nebraska (see Exhibit R) mention was made by the presenter of the upcoming approval of Kytril Tablets. A similar presentation was also made at another "Nurses Appreciation Night" held in Vermont (see Exhibit S). We also understand that these events are also being used to present misleading information about Zofran, including a claim that the longer half life of Kytril results in better efficacy than Zofran.

Obviously, there is, in our view, a high level of objectionable ongoing activity by SKB which must be addressed. We are prepared to seek redress of these concerns with the FDA or other appropriate body. However, we are willing initially to give you an opportunity to resolve our concerns prior to governmental involvement. I would like a satisfactory response to the issues raised here by February 10, 1995. Otherwise, we will move forward with our plans to raise these issues with DDMAC.

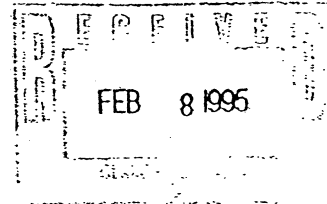
Sincerely,



Attachments

GWZ 313313

## **EXHIBIT B**



Via Facsimile  
and First Class Mail

February 7, 1995

Adrianna Carter  
Associate General Counsel  
Glaxo Inc.  
Five Moore Drive  
Research Triangle Park, NC 27709

Re: Promotional Complaint

Dear Ms. Carter:

This will confirm our telephone conversation of this morning regarding Tim Proctor's recent letter. In order for SB to perform any meaningful investigation of the claims made in that letter, we are in need of additional information. Specifically, in reference to the "homemade" materials that you reference as attachments "D" through "N" and "Q", we are interested in receiving information regarding (i) the location where these materials were allegedly left; (ii) the name of the physician or other healthcare professional to whom they were allegedly delivered; (iii) the date on which they were either delivered or retrieved; and (iv) the name of the SB representative, if known.

Use of "homemade" promotional materials is against SB policy. As I am sure that you can appreciate, if these materials are being generated by SB sales consultants, we are interesting in identifying them and taking appropriate disciplinary action. To that end, I will look forward to receiving any additional information that you may be able to provide.

Very truly yours,

A handwritten signature in dark ink, appearing to read 'Ursula B. Bartels'.

Ursula B. Bartels  
Vice President and  
Associate General Counsel

Appendix 5

Case 1:01-cv-12257-PBS Document 1634-2 Filed 08/03/05 Page 7 of 27

GWZ 314495

## **EXHIBIT C**



**SB**  
**SmithKline Beecham**

Ursula B. Bartels  
Vice President and Associate General Counsel

SENT VIA EXPRESS MAIL

February 22, 1995

Timothy D. Proctor  
Senior Vice President, General Counsel and Secretary  
Glaxo Inc.  
Five Moore Drive  
Research Triangle Park, NC 27709

Dear Tim:

This is in response to your letter to Charles Wakerley dated February 6, 1994 regarding Kytril promotion. First, permit me to say that we appreciate your bringing these matters to our attention. We are in agreement that self-policing on these matters is in the best interest of the industry. To that end, in addition to responding to your letter, I have taken this opportunity to alert you to some ongoing concerns of SB relating to Zofran promotion, including: a homemade cost comparison piece that is very similar to the ones to which you have objected; a Fraud & Abuse concern regarding non-hospital reimbursement; and a promotional concern relating to several symposia sponsored by your subsidiary, Cerenex.

Your letter was divided into four issues, which I will address in the order in which you raised them.

**1. Alleged Promotion of Unapproved Kytril Doses**

Your letter states that our promotional pieces contain data relating a 40 mcg./kg dose of Kytril. This was of concern to you since the approved dose of Kytril is 10 mcg./kg. As you may know, most of the clinical studies performed with Kytril were done with the 40 mcg dose. Dose ranging studies showed the doses of 10 mcg/kg and 40 mcg/kg to have comparable efficacy, and 10 mcg/kg was ultimately selected as the appropriate dosage. FDA has permitted us to use the 40 mcg data with appropriate statements, including the statement that "There was no statistically significant difference between the effect of these doses. Therefore the 10 mcg/kg was selected

SB04276

as the recommended dose." All FDA guidelines regarding the use of the 40 mcg. data were observed in the production of the pieces that you referenced in your letter. Indeed, two of the pieces, the launch sales aid and Slim Jim KY1014, were pre-cleared with DDMAC at the time of the launch.



## 2. "Homemade" Cost Comparisons

My concern over these "homemade" pieces, particularly the Fraud & Abuse considerations that you point out, prompted me to call you on the date that I received your letter. At your suggestion, I spoke to Glaxo Associate General Counsel Adrianna Carter, and requested that she facilitate our further investigation of these materials by providing us with any further details Glaxo might have regarding where the pieces were found, who created them, etc. I have confirmed this request to Ms. Carter in writing. Any help that you could provide would be most appreciated.

Without more information, we are unable to confirm that any of these materials were generated by our sales consultants. We are further unable to explore what was intended by the content of these materials in respect of reimbursement issues. Notwithstanding these qualifications, our concern over the possibility of such potential violations prompted us to issue a phonemail broadcast reminder to all SB sales consultants. On February 7, 1995, SB Vice President of Sales, Walter Graham, strongly reminded all SB consultants that the use of "homemade" promotional materials and/or any encouragement of improper billing practices by physicians are serious breaches of SB policy and could subject the violator to discipline, up to and including termination of employment. The phonemail was followed-up by a memo to sales management.

Regarding similar concerns, we would like to draw your attention to reports we are receiving from our field force regarding reimbursement issues. In an apparent effort to increase reimbursement to physicians and clinics, effective 1/10/95, Glaxo increased AWP for Zofran by 8.5%, while simultaneously fully discounting this increase to physicians. The latter was accomplished by a 14% rebate available to wholesalers on all non-hospital Zofran sales of the multi-dose vial. The net effect of these adjustments is to increase the amount of reimbursement available to physicians from Medicare and other third party payors whose reimbursement is based on AWP. Since the net price paid to Glaxo for the non-hospital sales of the Zofran multi-dose vial is actually lower, it does not appear that the increase in AWP was designed to increase revenue per unit to Glaxo. Absent any other tenable explanation, this adjustment appears to reflect an intent to induce physicians to purchase Zofran based on the opportunity to receive increased reimbursement from Medicare and other third party payors. In fact, we have had numerous verbal reports from the field concerning Glaxo representatives who

SB04277

are now selling Zofran based on the opportunity for physicians to receive a higher reimbursement from Medicare and other third-party payors while the cost to the physician of Zofran has not changed.

Attachment 1 is an example of the kind of "homemade" cost comparisons that were being disseminated in the field by Glaxo representatives prior to the recent change in AWP. The piece contains two overt factual inaccuracies that are misleading to the reader. First, Kytril is an infusion, not an IV push as suggested in the piece. Second, the Kytril "J" code went into effect January 1, 1995. We will provide you with any more recent examples that are picked up in the field. To the extent that details are available regarding any such materials, we will be happy to provide them to you in order to facilitate your investigation.

### 3. Promotion in Symposia and Conferences

Under this heading you reference slides from a presentation made by Dr. Carl Friedman nearly a year ago (March 10, 1994) in Puerto Rico. With respect to your concern regarding the use of 40 mcg. data in this presentation, please refer to the information set forth above in paragraph 1.

Dr. Friedman's objective in this presentation was to give oncologists a basic understanding of SB's clinical trials with Kytril Injection. To that end, the slides referenced SB's clinical trials of Kytril versus chlorpromazine/dexamethasone. As you may be aware, these trials are included in the Kytril labeling. Additionally, the slides from this talk received the benefit of review and comment by DDMAC in connection with a separate presentation by another presenter. The one item included in Dr. Friedman's talk that was absent from the materials that received FDA review was the slide on Kytril versus metoclopramide/dexamethasone. As part of this investigation of the concerns raised by your letter, we have drawn this slide to the attention of Dr. Friedman and our Kytril Product team. To the extent that it contains information that is not part of the permitted labeling, it will not be used for promotional purposes.

The unreferenced pricing information which you included as part of Exhibit "O" was not part of Dr. Friedman's presentation. We are treating that piece as part of the materials addressed in point 2, above.

The second program to which you objected under this heading is a symposium entitled "Chemotherapy Induced Nausea and Vomiting - Past and Present". This CE accredited program was presented by the Oncology Nurses Association ("ONA") in association with Scientific Therapeutics Information, Inc. ("STI") in connection with the Oncology Nursing Society's 19th Annual Congress on May 5, 1994.

SB04278

bcc:  
Walt Graham  
Bill DeVinney  
Howard Pien  
Jerry Karabelas  
Colleen Bennett  
Carl Friedman  
Olivia Pinkett  
Bob Powell  
Dick Van Thiel

SB04279

ZOFRAN AWP ~~\$214/40MG=\$5.35/MG~~  
\$171.20/32MG 80%(AWP)=\$136.96

KYTRIL AWP \$166/ML  
\$132.80/10McGM

ZOFRAN CONTRACT \$172/40MG=\$4.30MG  
\$137.60/32MG

ZOFRAN 32MG=\$137.60  
KYTRIL 10McGM=\$132.80 DIFF \$4.80

REIMB: ZF-CHEMO INFUSION 1HR (CODE 96410)  
\$44.95 X 80%=\$35.96  
KYTRIL IV PUSH \$25.90 X 80%=\$20.72  
DIFF REIMB \$15.24

Z-CODE ZOFRAN J-2405

KYTRIL CANNOT APPLY FOR J CODE TILL APRIL 1995 WILL  
BE JAN 1996 TO RECEIVE CODE

ZOFRAN MDV\* CONTAINS PRESERVATIVES\* CAN USE LEFTOVER  
MEDICATION AFTER 24HRS\* ELIMINATES ANY WASTE\*  
KYTRIL SDV\* MUST DISCARD AFTER OPENED IN 23HRS\*

MEDICARE FEE SCHEDULE RESTRICTIONS: MEMO AUG 1992  
SEPARATE PAYMENTS MAY BE MADE FOR EACH CHEMO AGENT  
FURNISHED ON DAY OF CHEMOTHERAPY ADMINISTERED USING  
HCPCS CODES TO BILL FOR DRUGS USED. IF, HOWEVER, MULTIPLE  
DRUGS ARE FURNISHED SEPARATELY, ONLY A SINGLE CHEMO  
THERAPY ADMINISTRATION CODE SHOULD BE USED. THEREFORE,  
IF MULTIPLE DRUGS ARE ADMINISTERED BY "PUSH" TECHNIQUE,  
ONLY ONE ADMINISTRATION CODE WILL BE RECOGNIZED.  
SIMILARLY, IN CASES WHERE CHEMOTHERAPY ADMINISTRATION  
FOR ONE DRUG IS BY INFUSION AND FOR ANOTHER DRUG BY  
PUSH, ONLY THE INFUSION CODE WILL BE REIMBURSED.  
\* reimbursement greater for infusion

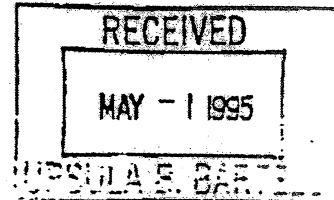
## **EXHIBIT D**

Glaxo

Adrianna L. Carter  
Assistant General Counsel

April 25, 1995

Ursula B. Bartels, Esq.  
Vice President and Associate  
General Counsel  
SmithKline Beecham  
One Franklin Plaza  
P.O. Box 7929  
Philadelphia, PA 19101



Dear Ms. Bartels:

This is in response to your February 22 letter to Timothy Proctor which was in response to a letter from Mr. Proctor dated February 6, 1995. We appreciate your prompt response and the actions you have taken to address some of the issues identified in Mr. Proctor's letter. However, it is clear from your letter, and we would agree, that several key issues remain unresolved. These issues are addressed below.

1. Promotion of Unapproved Kytril™ (granisetron HCL) Doses

Your response to our objection to the use of unapproved doses and the omission of fair balance in Kytril promotional pieces was that the FDA had essentially reviewed and approved the data presentations used to promote Kytril. This raises the issue of fairness for Glaxo since the FDA has recently objected to the distribution of dose ranging studies for Zofran® (ondansetron hcl) on the grounds that the studies contain unapproved doses. In addition, the FDA has apparently imposed upon Glaxo a more stringent standard for fair balance in promotional pieces. Given this, we will pursue these issues directly with DDMAC from the standpoint that the restrictions imposed on Zofran in these areas should be no more restrictive than those applicable to Kytril.

2. Distribution of "Homemade" Cost Comparisons

Attachment A is being provided in response to your request for additional information regarding the examples included in the February 6 letter of improper homemade cost

Ursula B. Bartels, Esq.  
 April 25, 1995  
 Page 2

comparisons distributed to health care professionals by SKB representatives. This attachment includes, where this information was available, the names of the cities where the homemade pieces (which were included as attachments to Mr. Proctor's February 6 letter) were discovered. In a few cases, we were able to identify and have provided to you the name of the SKB representative who left the materials. I have also included as Exhibit A1 a recent example of the type of homemade materials described in the February 6 letter. As you can see, this one includes the business card of the SKB representative who distributed the piece. This piece contains a price comparison that does not meet the standards set out by FDA. In addition, false and misleading statements are made about Zofran, including a statement that retreatment with tablets is required when Zofran is administered. Exhibit A2 is another example of an inappropriate price comparison. The comparison, along with a copy of a letter from M. D. Anderson Cancer Center and the antimetic guidelines for Sloan Kettering, were left by Stan Wallace of Decatur, Alabama with the Tennessee Valley Blood and Cancer Center. Exhibit A3 is another recent example left by an SKB representative in the Tidewater, Virginia area. Exhibit A4 which provides out of label stability information on Kytril was left recently by an SKB representative named Jack W. Griffith.

Your letter of February 22 included a homemade piece allegedly left with a healthcare professional by a Cerenex representative. As stated in your letter, it is difficult if not impossible to investigate these cases when no information as to the place and parties involved is provided. Therefore, we are requesting that any available information, including the place and date when the material was left, along with the name of the individual who allegedly left the piece, be provided to us. Glaxo has a strict policy prohibiting the use and/or distribution of homemade materials. Our representatives have been recently reminded of this policy by voice mail and through a written communication which required a written acknowledgment of their receipt and understanding of this policy. For this reason, we are particularly interested in the date this sheet was allegedly distributed.

### 3. Fraud and Abuse Issues

Your letter of February 22 states your concern regarding reimbursement issues associated with its recent price increase for Zofran Injection. According to this letter, "this [price] adjustment appears to reflect an intent to induce physicians to purchase Zofran based on the opportunity to receive increased reimbursement to Medicare. . . ." and Glaxo representatives "are now selling Zofran based on the opportunity for physicians to receive a higher reimbursement from Medicare and other third-party payers while the cost to the physician of Zofran has not changed." We do not agree with the implication that a routine, across the board price increase on a product represents illegal remuneration. It is true that, despite a price increase, some physicians and other healthcare professionals will not see the higher price as the result of rebates or other incentives. Any rebates or other incentives offered by Glaxo to



Ursula M. Bartels, Esq.  
 April 25, 1995  
 Page 3

providers comply with the requirements of Section 1128(b) of the Social Security Act applicable discount "safe harbor" regulations in 42 C.F.R. §1001.952 (h). It is also true that our sales representatives have been explaining the relationship between the price and Medicare reimbursement for Zofran to physicians. However, unlike SKB personnel, Glaxo representatives are not promoting Zofran on the grounds that the Medicare "profit" is more favorable than those for competing products.

In addition, SKB representatives have been instructing physicians to use one vial of Kytril for two or three patients and file claims indicating that they had in fact used one separate vial for each patient. This is reflected in some of the homemade pieces included in Tim Proctor's February 6 letter. We, nevertheless, appreciate the actions described in your letter to put an end to these activities. Unfortunately, despite your efforts, these activities are still ongoing. As an example, I have included as Exhibit A5 a copy of a homemade piece which was left by an SKB representative named M. J. Bartolomeo at a doctor's office in Michigan. The piece presents (incorrect) "profit" comparisons between Zofran and Kytril and also incorrectly indicates that Kytril is reimbursed at 100% while Zofran is reimbursed at the 80% level. The piece also recommends unapproved dosage levels for Kytril. Exhibit A6 includes examples of materials being left with physicians containing false and misleading comparisons between granisetron and Zofran.

#### 4. Promotion in Symposia and Conferences

The letter of February 7 also objected to a symposium entitled "Chemotherapy Induced Nausea and Vomiting-Past and Present." This symposium presented unapproved objectionable claims for Kytril, including comparative comparisons between Kytril and Zofran. Your response was that the symposium "conforms in all respects to the FDA's Draft Policy on Industry Supported Scientific and Educational Activities ("Draft Policy')." That policy states that the agency will not attempt to regulate programs that are educational and nonpromotional in nature. The Draft Policy also expresses a strong willingness to examine all relevant facts including the existence of a written agreement to determine if, in fact, a program is independent. Areas of inquiry would include the level of involvement of the supporting company of the program content and objectivity and balance "when a product marketed by the company or in competition with such product is to be the subject of substantial discussion."

The presentation given by Lorraine Baltzer Cleri as part of this symposium would not meet the standards set out by the FDA. Ms. Cleri's presentation was clearly a promotional discussion of Kytril. The introduction to the presentation includes statements such as, "Studies in the ferret have also shown that the duration of effect of granisetron is twice that seen with ondansetron." and "In this study, more patients preferred granisetron over the other two agents (P<.001)." The introduction and the slides also include extensive materials regarding a comparison of higher than approved

Ursula D. Bartels, Esq.  
 April 25, 1995  
 Page 4

doses of Kytril with lower than approved doses of Zofran. It is also obvious that some of Ms. Cleri's slides had been prepared by SKB. At least one of them can be found in the SKB-generated presentation of Dr. Friedman which was included in the February 6 letter to Mr. Wakerley as Exhibit "O". Given this, our position remains that SKB is improperly using company-sponsored symposia to disseminate inappropriate and misleading information on Zofran and Kytril. More recently, SKB representatives in the Cincinnati and Dayton, Ohio areas have used meetings, which included dinner and a Broadway show, to compare an out of label dose of Zofran (8 mg) with an out of label dose of Kytril (3 mg). The Pharm D making this presentation also included in the presentation a cost comparison between Zofran and Kytril. I have also included as Exhibit B a copy of a booklet entitled "Symposium Highlights Bulletin" which was mailed out to members of ASHP. The Bulletin contains highlights of a December 7, 1994 SKB sponsored ASHP symposium entitled "Therapeutic Consideration for Antiemetic Therapy in Oncology Patients." Like the symposium described above, this presentation appears to be nothing more than a promotional program for Kytril. Invalid or out of label information was presented on Kytril and Zofran. The summary ends with a discussion which purports to prove that granisetron is more cost effective than ondansetron. This is another example of a program that does not meet the FDA standards for independent programs.

Your February 22 letter indicates that you may have some concerns about the Glaxo symposia held during the same meeting as the one described above. Attached as Exhibit B1 is a copy of the pamphlet which described these symposia. These three symposia, entitled "The Cancer Experience in the Family," "Aggressive Cancer Treatment: Spotlight on Quality of Life," and "Nausea and Vomiting: Combining Holistic Care with Scientific Knowledge," met all the standards for independence and did not serve as vehicles to make promotional presentations on Zofran.

##### 5. Promotion of Kytril Tablets

Finally, your letter of February 22 requested additional information on the preapproval promotion of Kytril Tablets. The reprint entitled: Oral granisetron alone and in combination with dexamethasone: "A double-blind randomized comparison against high dose metoclopramide plus dexamethasone in prevention of cisplatin-induced emesis" which was included as Exhibit O of the February 6 letter was most recently left with an account in early February by Glenda Lewis, a SKB representative. I have also attached as Exhibit C a copy of a flyer handed out by an SKB representative named Phil Ra. As you can see, the flyer is an invitation to a presentation on Kytril Tablets. The Cincinnati/Dayton, Ohio meetings described above have also included a preapproval discussion on the use of Kytril Tablets.

SB01339

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Ursula B. Bartels, Esq.  
April 25, 1995  
Page 5

As stated previously, we do appreciate the response we have gotten to date to our concerns. I look forward to resolving the remaining issues in a similar, expeditious manner.

Very truly yours,

  
Adrianna L. Carter

ALC/mj

Attachments

18,  
/

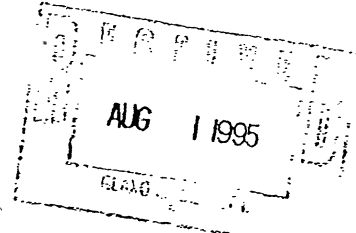
SB01340

**EXHIBIT A**

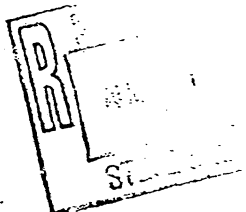
<u>Attachment</u>	<u>Area</u>	<u>SKB Rep</u>
D	Miami, VA	
E	Ocean County, NJ	
F	Denville, NJ	Heidi Haas
G	Escondido, CA	
H	Nashville, TN	
J	Brunswick, GA	
K	Taunton, MA	
L	Denville, NJ	Heidi Haas
M	Darien, IL	
N	Portland, OR (Kytril v. Zofran cost sheet) Philadelphia, PA  ("Monthly Cost Savings") Midland, TX  (Cost Calculator Sheet-Kytril) Ocean County, NJ	

SB04275

## **EXHIBIT E**



*File  
Zygen: Reg. mem.*



*cc: Mark Warner  
Tim Procter  
Dean Mitchell  
Steve Skoloff  
Chuck Bramley  
Rich Painter*

July 24, 1995

Adrianna L. Carter  
Assistant General Counsel  
Glaxo Wellcome  
Five Moore Drive  
Research Triangle Park, NC 27709

Dear Adrianna:

This supplements my letter to you of May 30, 1995, which was in reply to your correspondence of April 25, 1995. Much of the contents of your letter was a reprise of concerns raised in Mr. Procter's earlier correspondence, and has already been addressed in detail in my reply of February 22, 1995. Nevertheless, consistent with our internal policies, we conducted a review of the issues you raised in order to insure that our current promotional practices are consistent with applicable law and regulation.

First, regarding reimbursement issues, we appreciate your efforts to identify the individuals that were associated with the materials about which you have complained. We have confirmed that none of these materials, nor anything similar, is currently in use by the individuals identified, or as far as we have been able to determine, by any other employees of SB. Efforts continue to be undertaken by our management to insure that all promotional materials are consistent with FDA as well as other applicable laws and regulations, including the Anti-Kickback law.

Your letter continues to raise concerns about a symposia which took place at the Oncology Nursing Society's 19th Annual Congress on May 5, 1994. Specifically, you assert that certain scientific information which purportedly came from a presentation at that meeting "was clearly a promotional discussion of Kytril" and "would not meet the standards set out by FDA." To the contrary, as noted in our

GWZ 313559

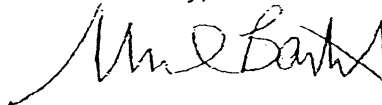
previous response, this symposium was conducted pursuant to a Grant Agreement that conforms in all respects to FDA's Draft Policy on Industry Supported Scientific and Educational Activities ("Draft Policy"). Consistent with that Draft Policy, ONA/STI had complete control over the content of the program, and the agreements specifically recite that "[t]he program will be independent of SB's influence".

Your letter raised a concern regarding purported distribution, in two instances, of an off-label journal article entitled "A Double-blind randomized comparison against high dose metoclopramide plus dexamethazone in prevention of cisplatin induced emesis". Although that journal article is available from our Product Information Department in response to unsolicited medical inquiries from physicians, it has not been distributed to the sales force for distribution. The copy that the field force received for background information was clearly marked across the front "Not for Distribution". Since that notation does not appear on the copy referenced in your letter as Exhibit "Q", it appears that the article was not in fact distributed by the SB field force, but was otherwise obtained by the physician.

Finally, you raise a concern about pre-approval promotion of Kytril Oral tablets based on a flyer attached to your letter as Exhibit "C". Because of the delay in FDA's approval of Kytril Oral, the meeting announced in Exhibit C focused exclusively on Kytril IV, and the oral was not mentioned.

In our view this closes the matters currently at issue.

Sincerely,

A handwritten signature in black ink, appearing to read "Ursula B. Bartels", with a stylized flourish at the end.

Ursula B. Bartels  
Vice President &  
Associate General Counsel

GWZ 313560

## **EXHIBIT F**





CAMBRIDGE LOS ANGELES PHOENIX [PLLC] SEATTLE

**hagens-berman.com**  
ONE MAIN STREET, 4<sup>TH</sup> FLOOR • CAMBRIDGE, MA 02142  
(617) 482-3700 • FAX (617) 482-3003

THOMAS M. SOBOL  
[tom@hagens-berman.com](mailto:tom@hagens-berman.com)

June 22, 2004

**VIA FACSIMILE**

Mark D. Seltzer  
Holland & Knight LLP  
10 St. James Avenue  
Boston, MA 02116

Re: In Re: Pharmaceutical Industry Average Wholesale Price Litigation MDL No. 1456

Dear Mark,

Enclosed is a deposition notice in the above-reference matter for each of Rich Franco, Virginia White, Steve Stefano, Al Goekan, George Esgro, Adriana Carter, Mike Yasick, Ron Sorrentino, Carl Pelzel, Peter Khalid, George Abercrombie and George Morrow. It is our understanding that you represent each of these individuals as current or former employees of GlaxoSmithKline. If this is not correct please notify me immediately so we can issue a separate subpoena.

I had discussed with you the need for deposition dates for each of these individuals but have not yet heard back from you with potential dates. The enclosed deposition notice is in compliance with the CMO 10 concerning the notice of depositions in this case. While it is always my policy to remain flexible and to work with opposing counsel to find mutually agreeable dates for depositions, the schedule for discovery set by the Court affords little flexibility. Please let me know immediately if there is a scheduling conflict with any of the noticed dates as well as any proposed alternative dates.

Very truly yours,

Thomas M. Sobol

Enclosure

cc: All counsel of record (Via VeriLaw)



UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF MASSACHUSETTS

IN RE PHARMACEUTICAL INDUSTRY	)	
AVERAGE WHOLESALE PRICE	)	MDL No. 1456
LITIGATION	)	
THIS DOCUMENT RELATES TO ALL	)	CIVIL ACTION: 01-CV-12257 PBS
CLASS ACTIONS	)	Judge Patti B. Saris
	)	

NOTICE OF DEPOSITIONS

TO: ALL COUNSEL BY VERILAW:

PLEASE TAKE NOTICE that, pursuant to Rule 30 of the Federal Rules of Civil Procedure, the undersigned counsel will take the depositions of the individuals listed below, all of who are employees of Defendant SmithKline Beecham Corp., d/b/a GlaxoSmithKline. Such depositions will be taken before a notary public or another officer authorized by law to administer oaths and will be recorded by stenographic means and/or by videotape, and will take place at the offices of Hagens Berman LLP, One Main Street, 4<sup>th</sup> Floor, Cambridge, Massachusetts, at the times and dates listed below.

Adriana Cortes	July 14, 2004	9:00 a.m.
George Esgro	July 15, 2004	9:00 a.m.
Al Goeken	July 16, 2004	9:00 a.m.
Steve Stefano	July 19, 2004	9:00 a.m.
Virginia White	July 20, 2004	9:00 a.m.
Rich Franco	July 28, 2004	9:00 a.m.
Mike Yasick	July 29, 2004	9:00 a.m.
Ron Sorrentino	August 2, 2004	9:00 a.m.
Carl Pezal	August 3, 2004	9:00 a.m.
Peter Khalid	August 4, 2004	9:00 a.m.
George Abercrombie	August 5, 2004	9:00 a.m.
George Marrow	August 6, 2004	9:00 a.m.



You are invited to attend and participate.

Dated: June 22, 2004

By: /s/ Thomas M. Sobol  
Thomas M. Sobol, Esq.  
**HAGENS BERMAN LLP**  
One Main Street, 4<sup>th</sup> Floor  
Cambridge, MA 02142  
Telephone: (617) 482-3700

### CERTIFICATE OF SERVICE

I, Thomas M. Sobol, certify that a true and correct copy of the notice of deposition for Adriana Cortes, George Esgro, Al Goeken, Steve Stefano, Virginia White, Rich Franco, Mike Yasick, Ron Sorrentino, Carl Pezal, Peter Khalid, George Abercrombie, and George Marrow was delivered to all counsel of record by electronic service pursuant to Paragraph 11 of the Case Management Order No. 2, by sending on June 22, 2004, a copy to Verilaw Technologies for Posting and notification to all parties

/s/ Thomas M. Sobol  
Thomas M. Sobol, Esq.  
**HAGENS BERMAN LLP**  
One Main Street, 4<sup>th</sup> Floor  
Cambridge, MA 02142  
Telephone: (617) 482-3700